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The title of the invention has been amended (Guidelines for Examination in the EPO, A-III, 7.3).

54 Food products enriched with nucleosides and/or nucleotides and preparation thereof.

57 Nourishing products enriched with nucleosides and/or nucleotides for infants and adults and processes for their preparation. The invention relates to milk and non-milk infant formulas, and nourishing products for adults, in which the addition of nucleosides and/or nucleotides provides enhanced effects and properties. Also the processes for the preparation of these products are described.

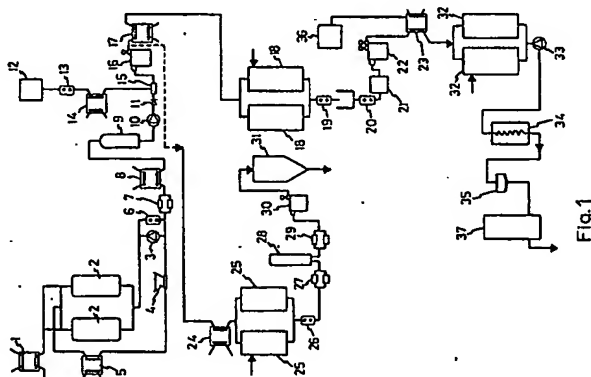


Fig. 1

Description

NOURISHING PRODUCTS ENRICHED WITH NUCLEOSIDES AND/OR NUCLEOTIDES FOR INFANTS AND ADULTS AND PROCESSES FOR THEIR PREPARATION

The present invention relates to the composition and the preparation of nourishing products suitable for both infants and adults, particularly when dietetic or physiological deficiencies are present. These products are enriched with nucleosides, nucleotides, or mixtures thereof.

More specifically, said products, which may be administered orally or by enteral feeding, are adapted milks for pre-term infants, initial milks, follow-up milks, dietetic products, lactose free dietetic products and hypoallergenic dietetic products.

The European Society of Pediatric Gastroenterology and Nutrition (ESPGAN), the American Academy of Pediatric (AAP), the Codex Alimentarius Mundi, and the European Community Council, among other international organizations, have given general rules for the composition of infant formulas (ESPGAN Committee on Nutrition, Acta Paed. Scand., Supl. 287, 1981; ESPGAN Committee on Nutrition, Acta Paed. Scand., Supl. 302, 1982; ESPGAN Committee on Nutrition, Acta Paed. Scand., Supl. 330, 1987; AAP Committee on Nutrition, Pediatric Nutrition Handbook, 1979; AAP Committee on Nutrition, Pediatrics, 75, 976, 1985; EEC Council, 85-C 28-05 COM (84) 703 in fine, 1985; EEC Council, 86-C 124-06 COM-86 91 in fine, 1986; Codex Alimentarius Mundi, Codex Stan. 72-1981).

As used in this description, the term -infant formulas- refers to the milk and non-milk substances for infant nutrition, particularly as defined by ESPGAN (Committee on Nutrition, Acta Paed. Scand., Supl. 262, pg. 3, supra) and also the AAP (Pediatrics, Vol. 57 n° 2, pg. 281, February 1976).

Infant formulas are derived, to a large extent, from cow's milk. After being diluted, cow's milk is enriched with serum proteins, diverse carbohydrates, such as lactose, dextrinmaltose and starches, different mixtures of vegetal and animal fats, vitamins and minerals, in suitable amounts to meet the requirements of low birth weight newborns or those of at-term healthy infants during the first and second semester of life.

Sometimes, infant formulas contain isolated milk proteins, isolated vegetal proteins or protein hydrolyzates, from different origins such as casein, lactalbumin, soy and meat. Also, these infant formulas have one or more carbohydrates (sucrose, dextrinmaltose and starches), mixtures of diverse kind of fats, minerals and vitamins, to meet not only the healthy newborns' nourishing requirements, but also of infants and children with symptoms of lactose intolerance, protein intolerance and, in general, with diverse malabsorption-malnutrition syndromes.

Usually, infant formulas tend to have a composition qualitatively and quantitatively as similar as possible to human milk. Nevertheless, despite the efforts made by several researchers, infant formulas still have a number of differences in their composition compared to human milk. This is because the latter has many substances, such as immunoglobulins, free amino acids, polyamines, nucleotides, polyunsaturated fatty acids, etc., which are not present in cow's milk. Thus it would be desirable that infant milk formulas have most of the substances present in human milk so as to produce the same physiological effects as human milk.

Regarding nutritional products for adults, specially for dietary purposes, even in hospitals, are based on the utilization of diverse protein sources (casein, sodium and calcium caseinates, isolated soy proteins, protein hydrolyzates and/or crystalline amino acids) mixtures of vegetal and animal fats, carbohydrates (basically glucose polymers), vitamins and minerals to meet, at least, the dietary intakes recommended for healthy individuals (Committee on Dietary Allowances, Food and Nutrition Board, Nat. Acad. Sci., 9th Ed, 1980).

Protein energy malnutrition (PEM) is found in many patients admitted to hospitals. This happens not only in developing countries, but also in those with a high socioeconomic level where the percentage of medical-surgical patients vary between 40-50 % (B. Bistrian et al. JAMA, 235, 1567, 1976; G. Hill et al. Lancet, 1, 689, 1977; Gassull et al. Human Nutr.: Clin. Nutr. 38C, 419, 1984). Proper nutritional support for such patients, while not a primary mode of treatment is, nevertheless, an important factor for therapy and recovery. It is, therefore important to administer a nutritionally balanced diet given orally, enterally or parenterally, adequate to the needs of the patient. This is specially true for those patients where conventional feeding is contraindicated (gastroenterological patients) or is insufficient (hypercatabolic patients). The enteral or oral mode of administration of foods is preferable to parenteral modes (E. Cabre and M.A. Gassull, J. Clin. Gastroenterol. Nutr., 1, 97, 1986) because of the lower morbidity, trophic effect upon the intestinal mucosa, lower necessity for instruments and lower costs.

Dietetic products for proper nourishment of patients are formulated to meet the requirements of those individuals in specific situations. Thus, complete balanced diets with an energy content between 130-150 Kcal/g nitrogen, are recommended for the preventive and repletive therapy in cases of PEM due to nervous anorexia, esophageal stenosis, maxillofacial surgery, chronic vasculo-cerebral disease, long evolution neurological syndromes, vascular surgery postoperative period, malabsorption syndromes, preoperative period, uncomplete intestinal occlusion, preparation of colon (surgery, radiology and endoscopy) and, in general, in all cases when it is necessary to take a balanced diet of nutrients. Diets with a high content of nitrogen (80-120 Kcal/g nitrogen) are recommended for the nutritional therapy of burn patients or patients suffering cranial trauma, multiple trauma, open fractures, Crohn disease, ulcerous colitis, digestive fistula, sepsis, oncology surgery, oncological radiotherapy and chemotherapy, pre- and postoperative periods, orthopedic surgery, and, in general, for catabolic patients.

Diets containing protein hydrolyzates as a source of amino nitrogen are specially made for the nutritional support of patients with diverse malabsorption-malnutrition syndromes, such as short bowel, acute celiac disease, Crohn disease, chronic pancreatic insufficiency, cystic fibrosis, intestinal fistulas, postoperative nutrition, and the like.

Furthermore, such products can be made as specific clinical diets for specific diseases, such as hepatopathies, chronic renal disease, and chronic obstructive pulmonary disease.

In addition, there is a variety of dietary products marketed to meet the nutritional needs of various individuals. For example, many individuals desirous of achieving varying degrees of weight loss, may benefit from the use of a special nutrition diet formulation to provide specific nutrients otherwise provided by a normal diet. Likewise, many people find it necessary to supplement their daily diet with additional nutrients due to age, allergy or physical afflictions.

As used herein, the terms diets, formulas and nutritionally balanced products are intended to refer to the aforementioned types of products.

Currently marketed nutrition products do not contain nucleic acids or their simpler compounds -nucleosides and/or nucleotides- which are normally present in foods and carry out fundamental physiological functions, described further on.

In relation to the nutritional importance of nucleotides, some relevant aspects of these compounds such as their content in human milk, physiological effects in newborns, intestinal absorption, tissue utilization and effects upon cell immunity are shown below.

U.S. Patent No. 4544559 teaches that human milk has a specific nucleotide content, very different from cow's milk. Human milk contains, at least, twelve different nucleotides, predominating CMP (cytidine monophosphate), AMP (adenosine monophosphate), UMP (uridine monophosphate), GMP (guanosine monophosphate), IMP (inosine monophosphate) and uridine derivatives, whereas cow's milk has very low amounts of CMP and AMP, it lacks the other nucleotides and has high amounts of orotic acid, which is absent in human milk.

Also, U.S. Patent No. 4544559 teaches that a humanized milk enriched with nucleotides (AMP, CMP, GMP, UMP, IMP) in the same range as human milk, stimulates the development of *Bifidobacterium bifidum* T1 at the intestinal level. This bacterium comprises 80 % of the total bifidobacteria present in the feces of breast-fed newborns. Furthermore, this humanized milk promotes a serum fatty acid profile very similar to that found in newborns fed with human milk.

U.S. Patent No. 3231385 describes infant milk formulas supplemented with certain nucleotides to simulate human milk, improve the milk taste and lower the curd tension.

Nucleotides can be synthesized in most tissues by two processes: (a) de novo synthesis from the precursors which include pirophosphoribosilphosphate, glutamine, aspartate, glycine, formate and carbon dioxide, and (b) utilization of the bases and nucleosides liberated through the catabolism of nucleotides and nucleic acids contained in foods. This last way, called salvage pathway, is an important alternative when biosynthetic de novo pathways are hindered by an insufficient supply of precursors. Tissues such as bone marrow, intestine and liver are heavily dependent on said salvage pathway. The activity of the salvage pathway has also been shown demonstrated in kidney, brain and retina.

The intestinal mucosa needs a continuous supply of nucleotides or their precursors from dietary origin, apart from the hepatic supply by the vascular system, in order to maintain continuous synthesis of RNA.

It has been confirmed in cuts made in the small intestine of rats that the exogenous ATP (adenosine triphosphate) increases the intracellular concentration of this nucleotide and it has been observed that at temperatures over 20° C the marked exogenous ATP is absorbed by everted sacs of rat small intestine. Also, it has been shown in rabbit's ileum "in vitro" that, at low concentrations, the ATP as well as the nucleoside adenosine are absorbed through a carrier associated to the enterocyte membrane.

Since the carrier system works for ATP and adenosine, it is likely that the system also works for other purine nucleotides, because competitive inhibition measures have proved that any compound with a purine ring united to a ribose molecule is absorbed.

It has also been shown that the purines and pyrimidines in the RNA and DNA, present in the diet, are absorbed by mice, preferably as nucleosides. Between 2-5 % of the nucleosides are used for nucleic acid synthesis in intestinal tissue, and cytosine nucleosides are used for DNA synthesis, specially in the spleen. Furtherly, it has been shown that purine bases, such as adenine, guanine, hypoxanthine and xantine are almost completely absorbed by rats, 4.5-6.5 % being incorporated in tissues and in a greater proportion by the liver and intestine.

The absence of pyrimidine or purine derivatives in the diet is known to suppress the normal function of T-lymphocytes (F. Rudolph et al. Adv. Exp. Med. Biol., 165,175, 1984), and to increase the mortality in experimental animals by staphylococcus sepsis. The addition of pyrimidine and purine derivatives to the diet decreases the susceptibility of animals to infection (A. Kulkarni et al, JPEN, 10, 169, 1986). Thus, the effect of purines and pyrimidines on the immune function can be of great importance in a number of clinic situations, such as transplants of organs in patients, malnutrition recovery, in diverse chemotherapeutic regimina and in the treatment of leukemias derived from T-cells.

Accordingly, one of the objects of the present invention is to provide improved nutritionally balanced diet formulations.

Another object of the present invention is to provide improved non-milk or milk based infant formulas which

not only closely resemble human milk, but which are more readily absorbed by the infant gut and enhance the infant's immune response. These and other objects of the present invention will become more apparent from the description which follows.

5 The present invention provides a range of compositions of infant formulas and adults nutrition products enriched with nucleosides, nucleotides or mixes of these two classes of compounds and the processes for their preparation. The products are in a liquid ready to eat form, or concentrated liquid or powder.

According to the invention, adenosine, guanosine, cytidine, inosine, and uridine or their mixes are used as nucleosides, and adenosine phosphate, guanosine phosphate, cytidine phosphate, inosine phosphate and uridine phosphate or their mixes are used as nucleotides.

10 The term uridine phosphate, guanosine phosphate, etc., is intended herein to refer collectively to the mono, di and/or tri phosphate as well as the sugar derivatives of the nucleotides mentioned. However, for various reasons which will be apparent to those knowledgeable in the art, the 5'-monophosphates are the preferred nucleotides.

15 The supplementation of nucleosides and/or nucleotides or their mixes to infant formulas and nutrition balanced diet formulations gives a better physiological fatty acid tissue membrane composition to newborns and adults, an improved cell immunity and a better intestinal repair in those individuals with intestinal diseases.

One embodiment of the present invention provides for a nutritionally balanced diet formulation which comprises a source of amino nitrogen, carbohydrates, edible fats, minerals, and vitamins, and at least one of the following nucleosides and/or nucleotides:

- 20 - uridine, uridine phosphate or a mixture thereof;
 - guanosine, guanosine phosphate or a mixture thereof;
 - adenosine, adenosine phosphate or a mixture thereof;
 - cytidine, cytidine phosphate or a mixture thereof, or
 - inosine, inosine phosphate or a mixture thereof.

25 Thus, the product must contain at least one of the fifteen different possible components. Generally, the product will contain from 1 to 300 mg (based on 100 grams of dry product) of the aforesaid components, with a preferred range being from about 50 to about 250 mg. The optimum amount appears to be about 150 mg per 100 grams of product.

30 On a liquid basis, these ranges correspond to from about 0.2 to 60 mg/dl, and preferably about 10 to about 50 mg/dl, with the optimum being about 30 ml/dl.

A further embodiment of the invention provides for improved non-milk infant formulas. Such non-milk formulas are well known and generally comprise carbohydrates, a source of amino acids, vegetable oils, minerals and vitamins. According to the invention, there is added to such formulas at least one of the following substances: uridine, uridine phosphate or mixtures thereof; guanosine, guanosine phosphate or mixtures thereof; adenosine, adenosine phosphate or mixtures thereof; cytidine, cytidine phosphate or mixtures thereof, or inosine, inosine phosphate or mixtures thereof.

35 As a minimum, at least about 0.27 mg per 100 g of product of one of said compounds should be added to the infant formula. Generally, the non-milk infant formulas according to the invention require on a dry weight basis in mg per 100 grams of product the following quantities:

- 40 - uridine and/or uridine phosphate 17.40-1.86 mg;
 - guanosine and/or guanosine phosphate 3.32-0.27 mg;
 - adenosine and/or adenosine phosphate 9.50-4.25 mg;
 - cytidine and/or cytidine phosphate 10.16-3.52 mg,
 and

- 45 - inosine and/or inosine phosphate 1.92-0.00 mg.

On a liquid basis, per dl, these formulations generally correspond as follows:

- 50 - uridine and/or uridine phosphate 2.62-0.28 mg;
 - guanosine and/or guanosine phosphate 0.50-0.04 mg;
 - adenosine and/or adenosine phosphate 1.43-0.64 mg;
 - cytidine and/or cytidine phosphate 1.53-0.53 mg,
 and

- inosine and/or inosine phosphate 0.29-0.00 mg.

For reasons discussed more fully below, it may be desirable to add small amounts of L-cistine and/or carnitine to the non-milk based infant formulas.

55 As yet a further embodiment of the invention there is provided an improved infant milk formula to which is added at least one nucleoside selected from the group consisting of uridine, guanosine, adenosine, cytidine and inosine.

The added nucleosides must be present in an amount about 0.27 mg per 100 grams of product on a dry basis. To provide for a closer simulation of human breast milk and also enhance absorption by the infant gut, there should be added to the infant milk formula the following approximate quantities for each 100 g of product:

- 60 - uridine and/or uridine phosphate 17.40-1.86 mg;
 - guanosine and/or guanosine phosphate 3.32-0.27 mg;
 - adenosine and/or adenosine phosphate 3.75-0.00 mg;
 65 - cytidine and/or cytidine phosphate 4.58-0.00 mg,

and

- inosine and/or inosine phosphate 1.92-0.00 mg.

On the following basis the corresponding quantities per dl will be as follows:

- uridine and/or uridine phosphate 2.62-0.28 mg;

- guanosine and/or guanosine phosphate 0.50-0.04 mg;

- adenosine and/or adenosine phosphate 0.56-0.00 mg;

- cytidine and/or cytidine phosphate 0.69-0.00 mg,

and

- inosine and/or inosine phosphate 0.29-0.00 mg.

Basically, infant formulas, according to the invention have a composition adequate for meeting the requirements of low birth weight infants, at term infants, children with lactose intolerance, children with cow's milk protein intolerance or children with diverse malabsorption syndromes.

The infants formulas and nutritionally balanced diet products of the present invention have been found to stimulate repair and regeneration of intestinal gut cells, enhance the immune response of T-cells and provide for specific fatty acid phospholipids profiles in red blood cell membranes.

The use of nucleosides is a characterizing feature of the products according to the invention. These materials generally have been found to be at least as effective as their corresponding nucleotides, and even more effective in providing for enhanced absorption through use of the salvage pathway in the human body. This action may be due to the higher water solubility of nucleosides as compared to the corresponding nucleotides. Also, nucleoside stability when used in the formulations of this invention is greater than that of the corresponding nucleotides.

When nucleosides and/or nucleotides or their combinations are added to infant formulas in concentrations in the same range as human milk, according to this invention, they stimulate the conversion of essential fatty acids to their polyunsaturated fatty acids (PUFA), which is reflected in the fatty acid composition of erythrocyte membrane both in the at-term newborn and in the pre-term newborn as well as in the fatty acids composition of plasma phospholipids.

In a study carried out by the inventors, 20 at-term newborns were fed exclusively on human milk, 19 with a conventional infant formula and 19 with the same infant formula supplemented with nucleotide-5'-monophosphates according to this invention, in similar concentrations to those of human milk. The relative content of PUFA, of the w6 series, derived from linoleic acid, as well as w3 series, derived from linolenic acid, was significantly decreased, specifically in phosphatidylethanolamine and phosphatidylserine of the erythrocyte membrane in infants fed conventional milk formula with respect to infants fed nucleotide-5'-monophosphates supplemented milk formula or human milk. The same happened in the plasma phospholipids and cholesterol esters. The arachidonic (20:4w6) and docosahexaenoic (22:6w3) acids were the most increased fatty acids in infants fed nucleotide-5'-monophosphates supplemented milk formula, with respect to those fed conventional milk formula.

In other study, 19 pre-term infants were fed exclusively on human milk, 18 with an infant milk formula for prematures and 18 with the same milk formula supplemented with nucleotides-5'-monophosphates in concentrations similar to those of human milk, according to this invention. At one month of live, the relative contents of eicosatrienoic acid (20:3w6), arachidonic acid (20:4w6), docosatetraenoic acid (22:4w6) and decosapentaenoic acid (22:5w6) were significantly decreased in the erythrocyte membrane phospholipids in infants fed milk formula with respect to those fed nucleotide-5'-monophosphate supplemented milk formula or human milk. Also, infants fed nucleotide-5'-monophosphate supplemented milk formula showed an intermediate value of docosahexaenoic acid (22:6w3) between those fed human milk and those fed milk formula. The same results were observed in the plasma phospholipids of pre-term newborns.

The modulating effect of nucleosides and nucleotides of the diet upon cell immunity has been proved through the following method:

Six groups of BALB-C mice, constituted by 10 mice each, aged four weeks, weaning period, were fed with a conventional diet, a nucleosides and nucleotides free diet, a diet supplemented with nucleosides according to this invention, in the following proportions: 50 mg of uridine, 50 mg of guanosine, 50 mg of adenosine, 50 mg of cytidine and 50 mg of inosine, a diet supplemented with nucleosides in proportions equivalent to mouse milk, a diet supplemented with 50 mg of the following nucleotides UMP, GMP, CMP, AMP and IMP according to this invention and a diet supplemented with nucleotides in proportions equivalent to mouse milk, respectively. The mice were fed during a period of four weeks, and it was carried out with them the testing of the cell immune response "in vitro" as response to allogeneic and syngeneic antigens using the lymphocyte mixed culture technique and quantifying the cell proliferation by the incorporation of 3H-thymidine to DNA and secondly was carried out the testing of the proliferation as response to phytohemagglutinin (mitogen agent) to quantify the state of lymphocyte reactivity, also with the incorporation of 3H-thymidine. The mice fed on the free nucleoside or nucleotide diets had an immune response mediated by T-cells lower than the other groups having a diet supplemented with these compounds.

The effects of nucleosides and nucleotides of the diet on the intestinal cell proliferation and on their enzymatic activity is proved as follows:

Two groups of Wistar mice, of 20 animals each, from the weaning (21 days of age), are fed during two weeks, the first of them on a diet (Diet A) containing 167 g of calcium caseinate, 489.5 g of corn starch, 150 g of sugar, 50 g of cellulose, 100 g of soy oil, 3 g of DL-methionin, 1.1 g of coline chloride, 38.2 g of a mineral mixture and

1.2 g of a vitamin mixture, per kg, to satisfy the nutritional requirements of these animals. The second group was fed with a similar diet, but with lactose instead of starch (Diet B). In this second group takes place an osmotic diarrhoea because of lactose intolerance giving rise to a malnutrition-malabsorption syndrome. Both groups are divided in two subgroups of 10 animals each, the first subgroup being fed on Diet A and the second with on Diet A supplemented with 50 mg of each of the following nucleosides: uridine, guanosine, adenosine, cytidine and inosine, during 4 weeks or with 50 mg of each of the following nucleotides: UMP, GMP, AMP, CMP and IMP, according to this invention.

The animals suffering malabsorption syndrome refed on the nucleoside or nucleotide supplemented diet, according to the invention, had ileal, jejunal and duodenal mucose weight significantly superior to those fed on a diet without such compounds. Also, the proportion of cells in a mitosis state, the mucose proteins content and the maltase and sucrase enzymatic activities were significantly higher in animals fed on the nucleoside or nucleotide supplemented diet than in those fed on a diet without such compounds.

Basic ingredients for infant formulas include cow's milk, proteins, whey proteins, casein and its salts (i.e. calcium caseinate); soy protein isolates are used in the products made for infants with lactose intolerance and/or cow's protein intolerance. Protein hydrolyzates (i.e. casein and lactalbumin hydrolyzates) with low molecular weight, may also be used for the products made for the treatment of infant malabsorption syndromes.

The proportions of the diverse component nutrients are similar to those of human milk. Thus, the ratio of whey proteins to casein currently varies from 60:40 to 70:30 in infant formulas based on milk. The mixture of fats employed is made up of edible fats to provide an essential fatty acids profile. Lactose is used exclusively as the carbohydrate source for at-term newborns infants, except that dextrinmaltose is employed in products used for the treatment of lactose intolerance and malabsorption syndromes in infancy.

Infant formulas according to the invention contain minerals (including calcium, phosphorus, sodium, potassium, chloride, magnesium, iron, zinc, copper, manganese and iodine) and vitamins (including vitamin A, D3, C, B1, B2, B6, B12, pantothenic acid, E, K1, folic acid, biotin) adequate for the infants' requirements. Also, in the products whose source of proteins is derived from soy or protein isolates or hydrolyzates, carnitine is included to satisfy the nutritional requirement for this compound in infants with malabsorptive syndromes.

The inventors of the present compositions and processes have demonstrated that the amounts of citosine, adenine, guanine, uracile and inosine derivatives in human milk, expressed as CMP, AMP, GMP, UMP and IMP, vary between 1.53-0.54, 1.43-0.69, 0.50-0.12, 2.62-1.40 and 0.29-0.00 mg/dl respectively and the individual contents of CMP, AMP, GMP, UMP and IMP oscillate between 1.73-0.53, 1.19-0.64, 0.21-0.04, 0.56-0.28, 0.29-0.00 mg/dl, respectively.

The content of nucleosides and/or nucleotides in the infant formulas of the present invention are in the range of those for human milk. An exemplary nucleoside and/or nucleotide mixture for infant formulas not containing cow's milk, according to the invention, is shown in Table I.

TABLE I

Content of nucleosides and/or nucleotides in infant formulas without cow's milk.

		Powdered product		Liquid product	
		Range		Range	
	Nucleosides and/or Nucleotides	mg/100g		mg/dl	
Uridine/Uridine phosphate	3.42	1.73	1.86	0.51	2.62-0.28
Guanosine/Guanosine phosphate	1.49	3.32	0.27	0.22	0.50-0.04
Adenosine/Adenosine phosphate	6.90	9.50	4.25	1.03	1.43-0.64
Cytidine/Cytidine phosphate	6.87	10.16	3.52	1.03	1.53-0.53
Inosine/Inosine phosphate	1.00	1.92	0.00	0.15	0.29-0.00

The amounts of adenosine and/or adenosine phosphate, cytidine and/or cytidine phosphate, inosine and/or inosine phosphate added to cow's milk based infant formulas, according to this invention, are lower than those shown in Table I, because cow's milk contains specific amounts of said compounds. Table II is an exemplary mixture of nucleosides and/or nucleotides for infant milk formulas containing cow's milk.

TABLE II

Content of nucleosides and/or nucleotides in infant formulas with cow's milk.

Nucleosides and/or Nucleotides	Powdered product	Liquid product	
	Range mg/100g	Range mg/dl	
Uridine/Uridine phosphate	17.40-1.86	2.62-0.28	5
Guanosine/Guanosine phosphate	3.32-0.27	0.50-0.04	10
Adenosine/Adenosine phosphate	3.75-0.00	0.56-0.00	15
Cytidine/Cytidine phosphate	4.58-0.00	0.69-0.00	20
Inosine/Inosine phosphate	1.92-0.00	0.29-0.00	25

The dietary products for balanced nutrition of adults, according to the invention, have a composition of nutrients adequate to the specific requirements of not only healthy human in need of a balanced nutritional product, but also those individuals in situations of energy-protein malnutrition and in hypercatabolic states derived from traumatic, septic, surgical processes and malabsorption syndromes.

As nitrogenous sources, the following components are preferably employed: a mixture of dairy proteins (casein or sodium and calcium caseinates and lactose free lactalbumin) and protein hydrolyzates with low molecular weight (maximum molecular weight 1,000 daltons, average molecular weight 500 daltons). As carbohydrate sources, glucose polymers are employed, such as dextrinmaltose with a different grade of dextrose equivalent degree, preferably between 10 and 30 DE. Fats are employed as a mixture of animal and one or more vegetable fats to meet the essential fatty acids requirements.

Nutritional products for adults according to the present invention provide mineral elements which include trace element and vitamins in adequate proportions to satisfy the specific requirements of normal healthy individuals as well as those suffering malabsorption-malnutrition processes and in a hypercatabolic state.

The nutritional products are enriched with nucleosides and/or nucleotides in similar amounts of nucleotides to those present in foods.

An example of a nucleoside and/or nucleotide mixture for the enrichment of nutritionally balanced products is shown in Table III.

TABLE III

Content of nucleosides and/or nucleotides in nutritionally balanced products for adults.

Nucleosides and/or Nucleotides	Powdered product		Liquid product		
	20	Range mg/100g	Range	mg/dl	
Uridine/Uridine phosphate	150	1-300	30	0.2-60	50
Guanosine/Guanosine phosphate	150	1-300	30	0.2-60	55
Adenosine/Adenosine phosphate	150	1-300	30	0.2-60	60
Cytidine/Cytidine phosphate	150	1-300	30	0.2-60	65
Inosine/Inosine phosphate	150	1-300	30	0.2-60	

On a dry weight basis, the amount of nucleosides and/or nucleotides may each vary from about 1 to about 300 mg per 100 grams of product, and preferably each ranges from about 50 to about 1,250 mg per 100 grams of product. On a liquid basis the amount may vary from about 0.2 to about 60 mg/dl of each nucleoside and/or nucleotide, and preferably ranges from about 10 to about 250 mg.

The invention also includes the processes to obtain infant formulas, as well as specific diets to be used in good nutrition, enriched with nucleosides and/or nucleotides.

The products can be prepared in liquid, ready to be used, concentrated to be diluted in water before its use, and in powder forms.

These processes comprise, in all cases, the preparation of a mixture containing water and non fat solids, except vitamins, some minerals and nucleosides and/or nucleotides, followed by a preheating to 75-80°C, deaeration of the mixture, injection of the fat mixture, double homogenization at 70-75°C (usually 150 kg/cm² in the first stage and 50 kg/cm² in the second) cooling to 4-6°C and storage in standardization tanks.

The liquid products ready for consumption or in concentrates to be diluted before use, are standardized in the said tanks, adapting the pH to values generally ranging from about 6.8 to about 7.1 and most preferably ranging from about 6.8 to 7.0 for infant formulas and from about 6.9 to 7.1 for nutritional products.

When the products are going to be UHT (ultra-high temperature) sterilized and aseptically packed in containers made of carton-aluminium-polyethylene, during the standardization, the vitamins, minerals and nucleosides or nucleotides mixtures are added as concentrated aqueous solutions and the content of mineral elements is adjusted by adding the required salts. The nucleoside and/or nucleotide solutions should be maintained preferably at pH 6-6.5 to avoid them to hydrolyze.

Once standardized, the products for consumption in liquid or concentrated forms, are sterilized through an UHT system at 145-150°C for 2-4 seconds and can be either aseptically packed or bottled in glass or polyethylene bottles. In the latter case, products are standardized prior to the UHT sterilization, only in their solids contents, and the pH is adjusted to values equivalents as noted above; immediately after they are sterilized, refrigerated at 4-6°C and stored in standardization tanks, the vitamins, minerals and the nucleoside and/or nucleotide solutions are added; afterwards the products are reheated at 30-70°C, packed in polyethylene or glass bottles, and sterilized in a continuous sterilizer at 120-121°C for 10 minutes.

In the case of powder products, after the phases of concentrated solids recombination, preheating, deaeration, fat mixture injection, homogenization, refrigeration, final pH standardization, concentration and addition of vitamins, minerals nucleosides and/or nucleotides, the mixture is reheated to 65-70°C, homogenized at 100-150 kg/cm² and dried in a spray drier. Afterwards, the powdered product is packed in polyethylene-aluminium containers or in cans, internally coated with varnish, under inert atmosphere, or in other acceptable containers.

A better understanding of the processes of the invention will be obtained from the detailed description which follows, given in relation to the accompanying drawing, in which:

Figure 1 is a schematic view of plant manufacturing process for preparing products of the present invention.

Following the schema of said figure, the general process and its alternatives are described in more detail below.

Through the heat exchanger (1), deionized water is fed to storage tanks (2), at a temperature between 60-70°C. Through the centrifugal pump (3) and tri-blender (4) non fat solids (proteins, carbohydrates and some materials) are dissolved being maintained the temperature at 60-65°C by means of heat exchanger (5).

The resulting mixture is fed through positive pump (6) to filters (7) and heat exchanger (8), to be heated to 75-80°C for 15-20 s to get the product pasteurized; being immediately deaerated in a vacuum deaerator (9), lowering the temperature to 70-75°C. Afterwards, the deaerated product is fed through centrifugal pump (10) and mixed with fat through fat injector (15). The mixture of fats stored in tank (12) has been fed through positive pump (13) to the heat exchanger (14) to be heated at 70-75°C before reaching fat injector (15). A retention valve (11) prevents the product which contains the non fat solids and fat to go back to the deaerator. Immediately after fats are mixed to the non fat solids mixture, the product is homogenized at (16) at a temperature of about 70-75°C and 200-300 kg/cm² of total pressure, in two stages (1st stage 150-200 kg/cm², 2nd stage 50-100 kg/cm²).

For liquid products which are to be aseptically packaged, after homogenization in (16), they are cooled to 4-6°C in plate heat exchanger (17) and fed to the pair of isothermal standardizing tanks (18) where the pH is adjusted to from about 6.8 to about 7.1 depending on the product desired. Vitamins, minerals, nucleosides and/or nucleotides in the required amounts are fed to (18) and the resulting mixture is fed by pumps (19) and (20) to a UHT sterilizer (21) at 145-150°C during 2-4 s, and homogenized in (22) (preferably in a double stage at 80°C and 200-250 kg/cm²), then is cooled to 20-25°C in heat exchanger (23) and aseptically packaged in (36), i.e. brick type packs of cardboard, aluminium and polyethylene.

For liquid products which are to be bottled, the process is the same as above through the cooling treatment in (17). Then the pH is adjusted in tanks (18) to above noted values. The mixture is fed by pumps (19) and (20) for UHT sterilization at (21) and homogenization at (22). The sterilized mixture is cooled in (23) and fed directly to standardizing tanks (32) where vitamins, minerals, nucleosides and/or nucleotides as required are added. From tanks (32), and by means of pump (33), the mixture is fed to reheater (34) where the temperature is raised to about 30°C for polyethylene bottles to 70°C for glass bottles. The product is bottled in a filling

machine (35) and subjected to sterilization in (37) at a temperature of about 120-121° C for about 10 to 15 minutes.

For powder products, the process is the same as above through homogenization in (16). As shown by the dotted line in the figure, the product is fed to heat exchanger (24) and cooled to about 4 to about 6° C and fed to isothermal standardizing tanks (25), where the pH is adjusted and the required vitamins, minerals, nucleosides and/or nucleotides are added. Then the standardized product is pumped by (26) through filters (27) and fed to reheater (28) where the temperature is raised to about 65 to about 70° C, and then filtered in (29) and homogenized at (30) under a pressure of about 100-200 kg/cm². The homogenized product is fed to a spray drying tower (31) and collected for packaging.

The invention will be readily understood from the following examples, which are not to be construed as limiting the scope of the invention.

EXAMPLE I

This example provides a product made to feed pre-term and low birth weight infants, enriched with nucleosides and/or nucleotides according to the invention. Basically, the product is a mixture of cow's milk, demineralized serum proteins, dextrinmaltose, fat mixture, minerals, vitamins and nucleosides and/or nucleotides mixture.

The product has been adapted in the proteins, fat carbohydrates, minerals and vitamins contents to the ESPGAN and AAP international recommendations as related to the feeding of low birth weight infants (ESPGAN, Committee on Nutrition, Acta Paediatr. Scand., 1987 (in press); AAP, Committee on Nutrition, Pediatrics, 1985).

TABLE IV

	For 100 g of powder	For 100 ml of liquid
Ingredients:		
Water	----	85 %
Maltodextrines	28.91 %	4.33 %
Vegetable oils mixture	20.23 %	3.03 %
Skim milk (0.05% fat)	14.58 %	2.19 %
Lactalbumin	12.13 %	1.82 %
Lactose	11.92 %	1.79 %
Butterfat	6.45 %	0.97 %
Minerals	3.26 %	0.49 %
Calcium caseinate	1.97 %	0.296 %
Lecithin	0.41 %	0.061 %
Vitamins	0.12 %	0.018 %
Nucleosides and/or nucleotides	0.0078%	0.0012%
Ascorbile palmitate	0.006 %	0.0009%
DL- α Tocopherol	0.001 %	0.0001%

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	3.42 mg	515 µg
Guanosine and/or guanosine monophosphate	1.49 mg	225 µg
Adenosine and/or adenosine monophosphate	1.32 mg	200 µg
Cytidine and/or cytidine monophosphate	1.12 mg	170 µg
Inosine and/or inosine monophosphate	0.45 mg	70 µg

Mineral salts added:

Calcium lactate	1.74 g	0.26 g
Sodium phosphate dibasic	0.65 g	97 mg
Calcium phosphate	0.36 g	54 mg
Potassium chloride	0.23 g	34 mg
Potassium phosphate dibasic	0.17 g	26 mg
Ferrous lactate	51.7 mg	7.6 mg
Magnesium sulfate	49 mg	7.3 mg
Zinc sulfate	7.3 mg	1.1 mg
Cupric sulfate	1.9 mg	285 µg
Sodium fluoride	1.5 mg	225 µg
Potassium and chromium sulfate	510 µg	76 µg
Sodium molybdate	265 µg	40 µg
Sodium selenite	180 µg	27 µg
Manganese sulfate	83 µg	12 µg
Potassium iodine	64 µg	10 µg

Vitamins added:

Vitamin A	1.600	UI	240	UI
Vitamin D	600	UI	90	UI
Vitamin E	5.5	mg	825	µg
Vitamin K	60	µg	9	µg
Thiamin	0.4	mg	60	µg
Riboflavin	0.45	mg	67	µg
Piridoxin	0.25	mg	37	µg
Niacin	6.7	mg	1	mg

Calcium pantothenate	5.5	mg	825	µg
Vitamin B12	1.1	µg	0.16	µg
Biotin	15	µg	2.2	µg
Folic acid	350	µg	52	µg
Vitamin C	100	mg	15	mg

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EXAMPLE II

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This example provides a milk formula made to feed at-term infants, during the first year of life, preferably for the 6 first months of lactation, supplemented with nucleosides and/or nucleotides in similar concentrations to those of human milk, according to the invention.

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The product has been adapted in its composition and content of nutrients to the ESPGAN and APP international recommendations for this kind of infants (ESPGAN, Committee on Nutrition, Acta Paediatr. Scand., suppl. 262, 1977; AAP, Committee on Nutrition, Pediatric Nutrition Handbook, 1979).

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TABLE V

	For 100 g of powder	For 100 ml of liquid
Ingredients:		
Water	----	87 %
Lactose	42.61 %	5.54 %
Vegetable oils	13.37 %	1.74 %
Powdered milk (26% fat)	25.47 %	3.31 %
Demineralized whey (65% proteins)	9.28 %	1.21 %
Butterfat	7.77 %	1.01 %
Mineral salts	1.11 %	0.14 %
Lecithin	0.31 %	0.04 %
Vitamins	0.069 %	0.009 %

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Nucleosides and/or nucleotides	0.0078%	0.001 %
Ascorbile palmitate	0.001 %	0.0001 %
DL- α Tocopherol	0.003 %	0.0004 %

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	3.42 mg	445 μ g
Guanosine and/or guanosine monophosphate	1.49 mg	195 μ g
Adenosine and/or adenosine monophosphate	1.32 mg	170 μ g
Cytidine and/or cytidine monophosphate	1.12 mg	145 μ g
Inosine and/or inosine monophosphate	0.45 mg	58 μ g

Mineral salts added:

Tricalcium citrate	0.31 g	40 mg
Tripotassium citrate	0.35 g	45 mg
Calcium chloride	0.16 g	21 mg
Dibasic potassium phosphate	0.24 g	31 mg
Ferrous lactate	39 mg	5.1 mg
Zinc acetate	8.5 mg	1.1 mg
Cupric sulfate	1.10 mg	143 μ g
Manganese sulfate	155 μ g	20 μ g
Potassium iodine	65 μ g	8.4 μ g

Vitamins added:

Vitamin A	1.600 UI	208 UI
Vitamin D	300 UI	39 UI
Vitamin E	5.5 mg	715 μ g
Vitamin K1	60 μ g	7.8 μ g
Calcium pantothenate	5.5 mg	715 μ g
Vitamin B12	1.1 μ g	0.14 μ g
Biotin	15 μ g	1.9 μ g
Folic acid	25 μ g	3.2 μ g
Vitamin C	50 mg	6.5 mg
Nicotinamide	6.7 mg	870 μ g

Vitamin B2	450	µg	58	µg
Vitamin B1	400	µg	52	µg
Vitamin B6	300	µg	39	µg

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EXAMPLE III

This example provides an infant milk formula made to feed healthy infants from 4-5 months to one year of live, supplemented with nucleosides and/or nucleotides, according to the invention. The product has been adapted in its composition and content of nutrients to the ESPGAN recommendations for these infants (ESPGAN, Committee on Nutrition, Acta Paediatr. Scan. Supl. 287,1981).

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TABLE VI

	For 100 g. of powder	For 100 ml of liquid
Ingredients:		
Water	----	85 %
Lactose	19.28 %	2.89 %
Vegetable oils mixture	6.08 %	0.91 %
Full milk	46.61 %	6.99 %
Maltodextrines	23.18 %	3.48 %
Demineralized whey	4.22 %	0.63 %
Mineral salts	0.41 %	0.061 %
Lecithin	0.14 %	0.021 %
Vitamins	0.069 %	0.01 %
Nucleosides and/or nucleotides	0.0078%	0.0012 %
Ascorbile palmitate	0.001 %	0.0001 %
DL- α Tocopherol	0.003 %	0.0004 %

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Nucleosides and/or nucleotides added:

5	Uridine and/or uridine monophosphate	3.42 mg	515 µg
	Guanosine and/or guanosine monophosphate	1.49 mg	225 µg
	Adenosine and/or adenosine monophosphate	1.32 mg	200 µg
10	Cytidine and/or cytidine monophosphate	1.12 mg	170 µg
	Inosine and/or inosine monophosphate	0.45 mg	70 µg

15 Mineral salts added:

	Monocalcium phosphate	0.36 g	54 mg
20	Ferrous lactate	39 mg	5.8 mg
	Zinc acetate	8.5 mg	1.3 mg
	Cupric sulfate	1.1 mg	165 µg
25	Manganese sulfate	155 µg	23 µg
	Potassium iodine	65 µg	9.7 µg

30 Vitamins added:

35 As in Example II.

40 EXAMPLE IV

45 This example provides a lactose free infant formula, containing protein from milk origin, supplemented with nucleosides and/or nucleotides in the same quantities as in human milk, according to the invention.

The product has been adapted in its composition and content of nutrients to the international recommendations mentioned before.

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TABLE VII

	For 100 g of powder	For 100 ml of liquid
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Ingredients:

Water	----	85	%
Vegetable oils mixture	10.35 %	1.55	%
Maltodextrines	58.03 %	8.7	%
Calcium caseinate + L-cistine	16.7 %	2.51	%
Butterfat	11.96 %	1.79	%
Mineral salts	2.18 %	0.33	%
Lecithin	0.69 %	0.103	%
Vitamins	0.069 %	0.01	%
Carnitine	0.0089%	0.0013	%
Nucleosides and/or nucleotides	0.0078%	0.0012	%
DL- α Tocopherol	0.003 %	0.0004	%
Ascorbile palmitate	0.001 %	0.0001	%

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	3.42 mg	515 μ g
Guanosine and/or guanosine monophosphate	1.49 mg	225 μ g
Adenosine and/or adenosine monophosphate	3.32 mg	500 μ g
Cytidine and/or cytidine monophosphate	4.98 mg	750 μ g
Inosine and/or inosine monophosphate	1.00 mg	150 μ g

Mineral salts added:

Dibasic potassium phosphate	588 mg	88 mg
Ferrous lactate	48 mg	7.2 mg
Tripotassium citrate	522 mg	78 mg
Zinc acetate	11.2 mg	1.7 mg
Cupric sulfate	1.15 mg	0.17 mg
Manganese sulfate	107 μ g	16 μ g
Potassium iodine	65 μ g	9.7 μ g

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Calcium lactate	272	mg	41	mg
Sodium chloride	389	mg	58	mg
Magnesium chloride	250	mg	39	mg

Vitamins added:

As in Example II.

Other substances added:

L-cistine	0.1 g	15	µg
Carnitine	8.9 mg	1.3	mg

EXAMPLE V

This example provides a lactose free adapted infant formula containing a protein isolate from vegetal origin, supplemented with nucleosides and/or nucleotides, according to the invention.

The product has been adapted, as in Example IV, in its composition and content of nutrients to the suckling children and newborns.

TABLE VIII

		For 100 g of powder	For 100 ml of liquid	
Ingredients:				
Water	----		85	%
Vegetable oils mixture	10.35	%	1.55	%
Maltodextrines	57.20	%	8.58	%
Soy protein isolate	16.67	%	2.5	%

Butterfat	11.96 %	1.79 %
Mineral salts	3.04 %	0.46 %
Lecithin	0.69 %	0.103 %
Vitamins	0.069 %	0.01 %
Carnitine	0.0089%	0.0013 %
Nucleosides and/or nucleotides	0.0078%	0.0012 %
Ascorbile palmitate	0.001 %	0.0001 %
DL- α Tocopherol	0.003 %	0.0004 %

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	3.42 mg	515 μ g
Guanosine and/or guanosine monophosphate	1.49 mg	225 μ g
Adenosine and/or adenosine monophosphate	3.32 mg	500 μ g
Cytidine and/or cytidine monophosphate	4.98 mg	750 μ g
Inosine and/or inosine monophosphate	1.00 mg	150 μ g

Mineral salts added:

Dibasic potassium phosphate	450 mg	67.5 mg
Ferrous lactate	48 mg	7.2 mg
Tripotassium citrate	628 mg	94.2 mg
Zinc acetate	11.2 mg	1.7 mg
Cupric sulfate	1.18 mg	0.18 mg
Manganese sulfate	107 μ g	25 μ g
Potassium iodine	65 μ g	9.7 μ g
Calcium lactate	873 mg	131 mg
Calcium chloride	370 mg	55.5 mg
Magnesium chloride	260 mg	39 mg
Calcium carbonate	400 mg	60 mg

Vitamins added:

As in Example II.

15 This example provides a lactose free infant formula which contains a mixture of lactalbumin and casein hydrolyzates with a low molecular weight, supplemented with nucleosides and/or nucleotides, as specified in the invention.

The composition and content of nutrients are adapted to the suckling children and newborns' requirements, as in Examples IV and V.

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	For 100 g	For 100 ml
.	of powder	of liquid

Ingredients:					
	Water	----		85	%
35	Vegetable oils mixture	16.98	%	2.55	%
	Maltodextrines	52.48	%	7.87	%
	Lactalbumin enzymatic hydrolyzate	12.31	%	1.85	%
40	Casein enzymatic hydrolyzate	5.16	%	0.77	%
	Corn starch	4.87	%	0.73	%
	Butterfat	4.29	%	0.64	%
45	Mineral salts	3.19	%	0.48	%
	Emulsifier	0.60	%	0.09	%
	Lecithin	0.0231	%	0.0035	%
50	Vitamins	0.069	%	0.01	%
	Carnitine	0.0089	%	0.0013	%
	Nucleosides and/or nucleotides	0.0078	%	0.0012	%

Ascorbile palmitate	0.0015%	0.0002 %
DL- α Tocopherol	0.0038%	0.0006 %

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	3.42 mg	515 μ g
Guanosine and/or guanosine monophosphate	1.49 mg	225 μ g
Adenosine and/or adenosine monophosphate	3.32 mg	500 μ g
Cytidine and/or cytidine monophosphate	4.98 mg	750 μ g
Inosine and/or inosine monophosphate	1.00 mg	150 μ g

Mineral salts added:

Dibasic potassium phosphate	0.12 g	18 mg
Ferrous lactate	39 mg	5.8 mg
Tripotassium citrate	0.85 g	0.13 g
Zinc acetate	10 mg	1.5 mg
Cupric sulfate	2.2 mg	330 μ g
Manganese sulfate	307 μ g	46 μ g
Potassium iodine	65 μ g	9.7 μ g
Calcium phosphate	0.86 g	0.13 g
Calcium chloride.	0.49 g	73 mg
Magnesium sulfate	0.20 g	30 mg
Sodium phosphate dibasic	0.38 g	57 mg
Potassium chloride	0.24 g	36 mg
Sodium fluoride	310 μ g	46.5 μ g
Potassium and chromium sulfate	115 μ g	17 μ g
Sodium molybdate	83 μ g	12 μ g
Sodium selenite	37 μ g	5.5 μ g

Vitamins added:

As in Example II.

Other substances added:

Carnitine	8.9 mg	1.3 mg
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The products in Examples IV, V and VI contain carnitine in similar concentration to that found in human milk, to satisfy the newborns' requirements of this compound.

The products in Examples I to VI are presented as liquid products, ready to use, as liquid concentrate products, to be used with the addition of water and as powdered products.

EXAMPLE VII

Example VII provides a complete product and nutritionally balanced to be used orally or by feeding tubes, with an energy ratio of 146 Kcal/g nitrogen, enriched with nucleosides and/or nucleotides in agreement with the invention.

The composition and content of nutrients have been adapted to the specific nutritional requirements of adults suffering energy-protein malnutrition.

TABLE X

		For 100 g of powder	For 100 ml of liquid	
Ingredients:				
Water	----		78.7	%
Vegetable oils mixture	12.1	%	2.5	%
Maltodextrines	52.13	%	11.2	%
Lactalbumin	11.63	%	2.48	%
Calcium caseinate	10.05	%	2.14	%
Butterfat	8.84	%	1.88	%
Mineral salts	3.79	%	0.79	%
Emulsifier	----		0.136	%
Stabilizer	----		0.02	%

Soy lecithin	0.66 %	----	
Vitamins	0.026 %	0.005 %	
Nucleosides and/or nucleotides	0.75 %	0.15 %	
Ascorbile palmitate	0.0232%	0.0008 %	
DL- α Tocopherol	0.0008%	0.0002 %	

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	150 mg	30 mg	
Guanosine and/or guanosine monophosphate	150 mg	30 mg	
Adenosine and/or adenosine monophosphate	150 mg	30 mg	
Cytidine and/or cytidine monophosphate	150 mg	30 mg	
Inosine and/or inosine monophosphate	150 mg	30 mg	

Mineral salts added:

Sodium phosphate dibasic	1.1 g	270 mg	
Ferrous lactate	21 mg	4 mg	
Dibasic potassium phosphate	0.28 g	34 mg	
Zinc acetate	14 mg	3 mg	
Cupric sulfate	3 mg	640 μ g	
Manganese sulfate	4 mg	760 μ g	
Potassium iodine	49 μ g	10 μ g	
Calcium chloride	0.31 g	58 mg	
Magnesium sulfate	1.014g	203 mg	
Potassium chloride	0.99 g	210 mg	
Sodium fluoride	2.2 mg	442 μ g	
Potassium and chromium sulfate	480 μ g	96 μ g	
Sodium molybdate	315 μ g	63 μ g	
Sodium selenite	166 μ g	33 μ g	
Sodium chloride	50 mg	6 mg	

Vitamins added:

Vitamin A	250 μ g	50 μ g	
Vitamin D	2.5 μ g	0.5 μ g	

	Vitamin E	2.5 mg	0.5 mg
	Vitamin K1	35 µg	7 µg
5	Pantothenic acid	1.75 mg	0.35 mg
	Vitamin B12	0.75 µg	0.15 µg
10	Biotin	50 µg	10 µg
	Folate	100 µg	20 µg
	Vitamin C	15 mg	3 mg
15	Niacin	4.75 mg	0.95 mg
	Vitamin B2	425 µg	85 µg
	Vitamin B1	375 µg	75 µg
20	Vitamin B6	550 µg	110 µg

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EXAMPLE VIII

30 This example provides a complete product and nutritionally balanced with a high protein content (91 Kcal/g nitrogen), enriched with nucleosides and/or nucleotides in agreement with the invention.

The composition and content of nutrients have been adapted to meet the specific nutritional requirements of adults in hypercatabolic state.

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TABLE XI

		For 100 g of powder	For 100 ml of liquid	
	Ingredients:			
45	Water	----	77.28	%
	Vegetable oils mixture	9.13 %	1.99	%
	Maltodextrines	50.6 %	11.49	%
50	Lactalbumin	15.96 %	3.64	%
	Calcium caseinate	13.08 %	3.14	%
	Butterfat	6.52 %	1.49	%
55	Mineral salts	3.41 %	0.68	%

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Emulsifier	----	0.11	%
Stabilizer	----	0.02	%
Soy lecithin	0.5 %	----	
Vitamins	0.026 %	0.005	%
Nucleosides and/or nucleotides	0.75 %	0.15	%
Ascorbile palmitate	0.0232%	0.0008	%
DL- α Tocopherol	0.0008%	0.0002	%

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	150	mg	30	mg
Guanosine and/or guanosine monophosphate	150	mg	30	mg
Adenosine and/or adenosine monophosphate	150	mg	30	mg
Cytidine and/or cytidine monophosphate	150	mg	30	mg
Inosine and/or inosine monophosphate	150	mg	30	mg

Mineral salts added:

Sodium phosphate dibasic	0.88 g	180	mg
Ferrous lactate	21 mg	4	mg
Dibasic potassium phosphate	0.19 g	30	mg
Zinc acetate	14 mg	3	mg
Cupric sulfate	3 mg	640	μ g
Manganese sulfate	4 mg	760	μ g
Potassium iodine	49 μ g	10	μ g
Calcium chloride	0.11 g	5	mg
Magnesium sulfate	1.014g	203	mg
Potassium chloride	1.01 g	220	mg
Sodium fluoride	2.2 mg	442	μ g
Potassium and chromium sulfate	480 μ g	96	μ g
Sodium molybdate	315 μ g	63	μ g
Sodium selenite	166 μ g	33	μ g
Sodium chloride	0.16 g	40	mg

Vitamins added:

5 As in Example VII.

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EXAMPLE IX

15 This example provides a complete product and nutritionally balanced, with a high nitrogen content, using as source of this element a protein hydrolyzate with a low molecular weight to make easier its absorption, enriched with nucleosides and/or nucleotides according to the invention. The energy ratio of this product is 100 Kcal/g nitrogen.

20 The composition and content of nutrients have been adapted to satisfy the specific nutritional requirements of adults suffering diverse malabsorption-malnutrition syndromes.

TABLE XII

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		For 100 g	For 100 ml	
		of powder	of liquid	
30	Ingredients:			
	Water	----	77.83	%
35	Vegetable oils mixture	12.44 %	2.76	%
	Maltodextrines	51.62 %	11.43	%
	Casein hydrolyzate	25.80 %	5.72	%
40	Butterfat	3.62 %	0.8	%
	Mineral salts	5.02 %	1.11	%
	Emulsifier	----	0.11	%
45	Stabilizer	----	0.02	%
	Soy lecithin	0.50 %	----	
	Vitamins	0.026 %	0.0058	%
50	Nucleosides and/or nucleotides	0.75 %	0.17	%
	L-cistine	0.20 %	0.04	%

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Ascorbile palmitate	0.0232%	0.0051 %
DL- α Tocopherol	0.0008%	0.0002 %

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	150 mg	30 mg
Guanosine and/or guanosine monophosphate	150 mg	30 mg
Adenosine and/or adenosine monophosphate	150 mg	30 mg
Cytidine and/or cytidine monophosphate	150 mg	30 mg
Inosine and/or inosine monophosphate	150 mg	30 mg

Mineral salts added:

Sodium phosphate dibasic	1.05 g	233 mg
Ferrous lactate	21 mg	4.6 mg
Dibasic potassium phosphate	0.80 g	177 mg
Zinc acetate	14 mg	3.1 mg
Cupric sulfate	3 mg	665 μ g
Manganese sulfate	4 mg	888 μ g
Potassium iodine	49 μ g	11 μ g
Calcium chloride	0.84 g	186 mg
Magnesium sulfate	1.014g	225 mg
Sodium fluoride	2.2 mg	488 μ g
Potassium and chromium sulfate	480 μ g	106 μ g
Sodium molybdate	315 μ g	70 μ g
Sodium selenite	166 μ g	37 μ g
Sodium chloride	0.44 g	97 mg
Tripotassium citrate	0.83 g	184 mg

Vitamins added:

As in Example VII.

Other substances added:

L-cistine	200 mg	40 mg
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EXAMPLE X

This example provides a complete product and nutritionally balanced with a low protein content, supplemented with branched chain amino acids and enriched with nucleosides and/or nucleotides, according to the invention.

The composition and content of nutrients have been adapted to satisfy the specific nutritional requirements of adults suffering severe hepatopathy.

TABLE XIII

		For 100 g of powder	For 100 ml of liquid	
Ingredients:				
Water	----		76.36	%
Vegetable oils mixture	7.48	%	1.77	%
Maltodextrines	72.13	%	17.04	%
Lactalbumin	7.26	%	1.72	%
Calcium caseinate	6.27	%	1.48	%
Mineral salts	2.94	%	0.69	%
Emulsifier	----		0.05	%
Stabilizer	----		0.01	%
Soy lecithin	0.22	%	----	
Vitamins	0.026	%	0.006	%
Nucleosides and/or nucleotides	0.75	%	0.18	%
L-leucine	1.16	%	0.27	%
L-valine	0.87	%	0.21	%
L-isoleucine	0.87	%	0.21	%
Ascorbile palmitate	0.0197	%	0.005	%
DL- α Tocopherol	0.0003	%	0.00007	%

Nucleosides and/or nucleotides added:

Uridine and/or uridine monophosphate	150	mg	30	mg
Guanosine and/or guanosine monophosphate	150	mg	30	mg
Adenosine and/or adenosine monophosphate	150	mg	30	mg
Cytidine and/or cytidine monophosphate	150	mg	30	mg
Inosine and/or inosine monophosphate	150	mg	30	mg

Mineral salts added:

Sodium phosphate dibasic	0.60	g	142	mg
Ferrous lactate	21	mg	5	mg
Dibasic potassium phosphate	0.67	g	158	mg
Zinc acetate	14	mg	3.3	mg
Cupric sulfate	3	mg	709	µg
Manganese sulfate	4	mg	946	µg
Potassium iodine	49	µg	11.6	µg
Calcium chloride	0.49	g	116	mg
Magnesium sulfate	1.014	g	240	mg
Sodium fluoride	2.2	mg	520	µg
Potassium and chromium sulfate	480	µg	113	µg
Sodium molybdate	315	µg	74	µg
Sodium selenite	166	µg	39	µg
Sodium chloride	0.12	g	28	mg

Vitamins added:

As in Example VII.

Other substances added:

L-leucine	1.16	g	274	mg
L-valine	870	mg	206	mg
L-isoleucine	870	mg	206	mg

EXAMPLE XI

This example provides a product considered as a nutritional supplement for the nutritional repletion of adults with chronic hepatopathy, constituted by a mixture of proteins from milk origin, supplemented with branched chain amino acids, carbohydrates vitamins and minerals and enriched with nucleosides and/or nucleotides.

TABLE XIV

		For 100 g of powder	For 100 ml of liquid	
Ingredients:				
Water	----		90.00	%
Maltodextrines	36.72	%	7.32	%
Lactalbumin	26.26	%	5.25	%
Sodium caseinate	21.95	%	4.39	%
Mineral salts	3.2	%	0.64	%
Vitamins	0.026	%	0.005	%
Nucleosides and/or nucleotides	0.75	%	0.15	%
L-leucine	4.04	%	0.81	%
L-valine	3.03	%	0.61	%
L-isoleucine	3.03	%	0.61	%
Nucleosides and/or nucleotides added:				
Uridine and/or uridine monophosphate	150	mg	30	mg
Guanosine and/or guanosine monophosphate	150	mg	30	mg
Adenosine and/or adenosine monophosphate	150	mg	30	mg
Cytidine and/or cytidine monophosphate	150	mg	30	mg
Inosine and/or inosine monophosphate	150	mg	30	mg

Mineral salts added:

Sodium phosphate dibasic	0.36 g	72	mg	5
Ferrous lactate	21	mg	4.2	mg
Dibasic potassium phosphate	0.17 g	34	mg	
Zinc acetate	14	mg	2.8	mg 10
Cupric sulfate	3	mg	600	µg
Manganese sulfate	4	mg	800	µg
Potassium iodine	49	µg	9.8	µg 15
Calcium chloride	0.38 g	76	mg	
Magnesium sulfate	1.014g	203	mg	
Sodium fluoride	2.2	mg	440	µg 20
Potassium and chromium sulfate	480	µg	96	µg
Sodium molybdate	315	µg	63	µg
Sodium selenite	166	µg	33	µg 25
Potassium chloride	0.89 g	178	mg	
Tripotassium citrate	0.34 g	68	mg	30

Vitamins added:

As in Example VII.

Other substances added:

L-leucine	4.04	g	810	mg	
L-valine	3.03	g	610	mg	45
L-isoleucine	3.03	g	610	mg	

The invention having been thus described, it will be appreciated by those in the art that variations can occur within the scope of claims which follow.

Claims

1. A nutritionally balanced nourishing product, which contains a source of amino nitrogen, carbohydrates, edible fats, minerals, and vitamins characterized by comprising at least one nucleoside selected from the group consisting of uridine, guanosine, adenosine, cytidine and inosine.

2. A nutritionally balanced nourishing product, according to claim 1, in powder form, characterized by containing for each 100 g:

- uridine 1-300 mg;
- guanosine 1-300 mg;
- adenosine 1-300 mg;

- cytidine 1-300 mg, and
- inosine 1-300 mg.

3. A nutritionally balanced nourishing product, according to claim 2, characterized by containing:

- uridine 50-250 mg;
- guanosine 50-250 mg;
- adenosine 50-250 mg;
- cytidine 50-250 mg, and
- inosine 50-250 mg.

4. A nutritionally balanced nourishing product, according to claim 1, in liquid form, characterized by containing per deciliter:

- uridine 0.2-60 mg;
- guanosine 0.2-60 mg;
- adenosine 0.2-60 mg;
- cytidine 0.2-60 mg, and
- inosine 0.2-60 mg.

5. A nutritionally balanced nourishing product, according to claim 4, characterized by containing:

- uridine 10-50 mg;
- guanosine 10-50 mg;
- adenosine 10-50 mg;
- cytidine 10-50 mg, and
- inosine 10-50 mg.

6. A nutritionally balanced nourishing product in powder form, which contains a source of amino nitrogen, carbohydrates, edible fats, minerals and vitamins, characterized by also containing a nucleoside/nucleotide composition comprising at least one of:

- uridine, uridine phosphate or mixtures thereof;
- guanosine, guanosine phosphate or mixtures thereof;
- adenosine, adenosine phosphate or mixtures thereof;
- cytidine, cytidine phosphate or mixtures thereof, or
- inosine, inosine phosphate or mixtures thereof,

wherein the total combined nucleoside and nucleotide content of said composition is in the range of between about 50 to about 1.250 mg for each 100 g of product.

7. A nutritionally balanced nourishing product in liquid form, which contains a source of amino nitrogen, carbohydrates, edible fats, minerals and vitamins, characterized by also containing a nucleoside/nucleotide composition comprising at least one of:

- uridine, uridine phosphate or mixtures thereof;
- guanosine, guanosine phosphate or mixtures thereof;
- adenosine, adenosine phosphate or mixtures thereof;
- cytidine, cytidine phosphate or mixtures thereof, or
- inosine, inosine phosphate or mixtures thereof,

wherein the total combined nucleoside and nucleotide content of said composition is in the range of between about 10 to about 250 mg for each 100 g of product.

8. A cow's milk exempt infant formula comprising carbohydrates, a source of amino acids, vegetable oils, minerals and vitamins, characterized by comprising at least one of the following substances:

- uridine, uridine phosphate or mixtures thereof;
- guanosine, guanosine phosphate or mixtures thereof;
- adenosine, adenosine phosphate or mixtures thereof;
- cytidine, cytidine phosphate or mixtures thereof, or
- inosine, inosine phosphate or mixtures thereof.

9. A cow's milk except infant formula, according to claim 8, characterized by comprising on a dry basis per 100 g:

- 0.00-17.40 mg of uridine, uridine phosphate or mixtures thereof;
- 0.00-03.32 mg of guanosine, guanosine phosphate or mixtures thereof;
- 0.00-03.75 mg of adenosine, adenosine phosphate or mixtures thereof;
- 0.00-04.58 mg of cytidine, cytidine phosphate or mixtures thereof, and
- 0.00-01.92 mg of inosine, inosine phosphate or mixtures thereof.

10. A cow's milk except infant formula, according to claim 8, characterized by its powdered form.

11. A cow's milk exempt infant formula, according to claim 9, characterized by containing per 100 g of total weight:

- uridine and/or uridine phosphate 17.40-1.86 mg;
- guanosine and/or guanosine phosphate 3.32-0.27 mg;
- adenosine and/or adenosine phosphate 9.50-4.25 mg;
- cytidine and/or cytidine phosphate 10.16-3.52 mg, and
- inosine and/or inosine phosphate 1.92-0.00 mg.

12. A cow's milk exempt infant formula, according to claim 8, characterized by its liquid form.

13. A cow's milk exempt infant formula, according to claim 12, characterized by containing per deciliter

of liquid product:

- uridine and/or uridine phosphate 2.62-0.28 mg;
- guanosine and/or guanosine phosphate 0.50-0.04 mg;
- adenosine and/or adenosine phosphate 1.43-0.64 mg;
- cytidine and/or cytidine phosphate 1.53-0.53 mg, and
- inosine and/or inosine phosphate 0.29-0.00 mg. 5
- 14. A cow's milk exempt infant formula, according to claim 9, characterized by containing L-cistine.
- 15. A cow's milk exempt infant formula, according to claim 11, characterized by containing L-cistine.
- 16. A cow's milk exempt infant formula, according to claim 9, characterized by containing carnitine.
- 17. A cow's milk exempt infant formula, according to claim 11, characterized by containing carnitine. 10
- 18. An infant milk formula containing cow's milk, sugars, vegetable oils, minerals and vitamins, characterized by comprising at least one nucleoside selected from the group consisting of uridine, guanosine, adenosine, cytidine and inosine.
- 19. An infant formula, according to claim 18, characterized by also containing at least one nucleotide selected from the group consisting of uridine phosphate, guanosine phosphate, adenosine phosphate, cytidine phosphate and inosine phosphate. 15
- 20. An infant formula, according to claim 18, characterized by comprising:
 - uridine, uridine phosphate or a mixture thereof;
 - guanosine, guanosine phosphate or a mixture thereof;
 - adenosine, adenosine phosphate or a mixture thereof;
 - cytidine, cytidine phosphate or mixture thereof, and
 - inosine, inosine phosphate or a mixture thereof.
 20
- 21. An infant formula, according to claim 18, characterized by containing for each 100 g of powder product:
 - uridine and/or uridine phosphate 17.40-1.86 mg;
 - guanosine and/or guanosine phosphate 3.32-0.27 mg;
 - adenosine and/or adenosine phosphate 3.75-0.00 mg;
 - cytidine and/or cytidine phosphate 4.58-0.00 mg, and
 - inosine and/or inosine phosphate 1.92-0.00 mg.
 25
- 22. An infant formula, according to claim 18, characterized by containing per deciliter of liquid product:
 - uridine and/or uridine phosphate .262-0.28 mg;
 - guanosine and/or guanosine phosphate 0.50-0.04 mg;
 - adenosine and/or adenosine phosphate 0.56-0.00 mg;
 - cytidine and/or cytidine phosphate 0.69-0.00 mg, and
 - inosine and/or inosine phosphate 0.29-0.00 mg.
 30
- 23. Process for the preparation in liquid form and aseptic packaging of nourishing products enriched with nucleosides and/or nucleotides, having a composition according to claims 1, 4, 5, 7, 8, 12, 13, 18, 19, 20 and 22, characterized by comprising the steps of:
 - Mixing water and non-fat solids, in the absence of any vitamins, nucleosides and nucleotides;
 - Preheating the mixture to a temperature ranging from about 75 to about 80° C;
 - Deaerating of the said mixture;
 - Injection of a mixture of edible fats in the deaerated mixture;
 - Homogenizing the mixture under pressure;
 - Cooling of the mixture in the range of about 4-6° C;
 - Standardizing the mixture by addition of those nucleosides, nucleotides, vitamins, minerals and other components not added in first step, adjusting the pH in the range of about 6.8 to about 7.1;
 - UHT sterilizing of the standardized mixture;
 - Homogenizing of the mixture under pressure followed by cooling, and
 - Aseptic packaging of the obtained product.
 35
- 24. Process for the preparation in liquid form and bottling of nourishing products enriched with nucleosides and/or nucleotides, having a composition according to claims 1, 4, 5, 7, 8, 12, 13, 18, 19, 20 and 22, characterized by comprising the steps of:
 - Mixing water and non-fat solids, in the absence of any vitamins, nucleosides and nucleotides;
 - Preheating the mixture to a temperature ranging from about 75 to about 80° C;
 - Deaerating of the said mixture;
 - Injection of a mixture of edible fats in the deaerated mixture;
 - Homogenizing the mixture under pressure;
 - Cooling of the mixture in the range of about 4-6° C;
 - Adjusting pH in the range of about 6.8 to about 7.1;
 - UHT sterilizing of the adjusted mixture;
 - Standardizing of the sterilized mixture by addition of those nucleosides, nucleotides, vitamins, minerals and other components not added in first step;
 - Reheating of the standardized mixture to about 30-70° C;
 - Bottling of the reheated mixture, and
 - Sterilizing the final bottled product.
 40

25. Process for the preparation in powder form of nourishing products enriched with nucleosides and/or nucleotides, having a composition according to claim 1, 2, 3, 6, 8, 9, 10, 11, 14, 15, 16, 17, 18, 19, 20 and 21, characterized by comprising the steps of:

- Mixing water with the non-fat solids, in the absence of the vitamins, nucleosides and nucleotides;
- Preheating the mixture to a temperature ranging from about 75 to about 80° C;
- Deaerating of the said mixture ;
- Injection of a mixture of edible fats in the deaerated mixture;
- Homogenizing the mixture under pressure;
- Cooling of the mixture in the range of about 4-6° C;
- Standardizing of the cooled mixture by addition of those nucleosides, nucleotides, vitamins, minerals and other components not added in first step, adjusting the pH in the range of about 6.8 to about 7.1;
- Reheating of the standardized mixture to between about 65 to about 70° C;
- Homogenizing of the reheated mixture under pressure;
- Drying in a spray drier, and
- Packaging of the obtained product.

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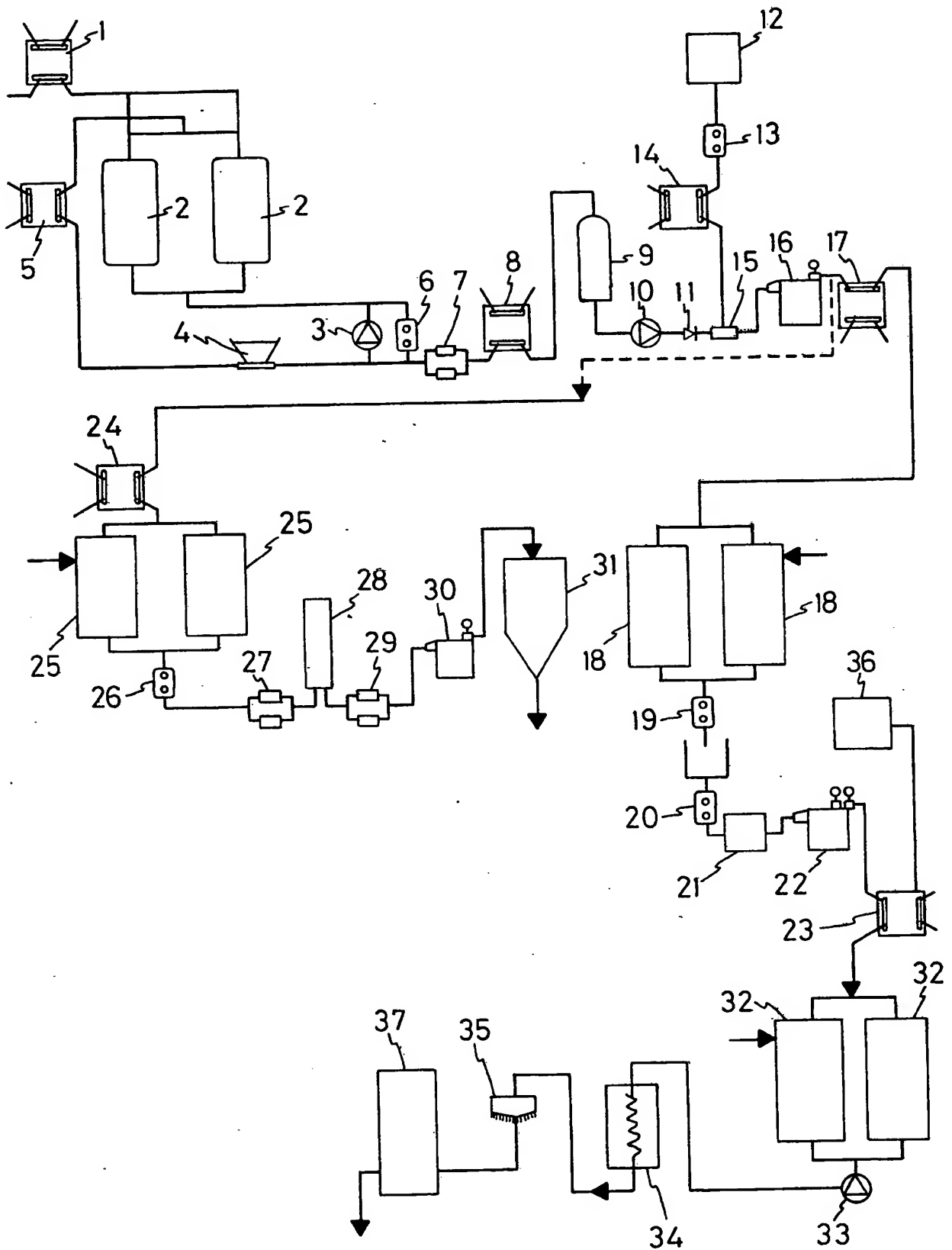


Fig.1

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